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NOTICE OF ALLOWANCE AND FEE(S) DUE

000022195 7590 02/20/2004

HUMAN GENOME SCIENCES INC
14200 SHADY GROVE ROAD
ROCKVILLE, MD 20850

EXAMINER	
ROBINSON, HOPE A	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/20/2004

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,041	04/12/2001	Craig A. Rosen	6832.0016	2391

TITLE OF INVENTION: ALBUMIN FUSION PROTEINS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1330	$300	$1630	05/20/2004

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

☐ Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 11/03) Approved for use through 04/30/2004.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

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ROCKVILLE, MD 20850

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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EXAMINER	ART UNIT	CLASS-SUBCLASS
ROBINSON, HOPE A	1653	435-069700

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent); ❑ individual ❑ corporation or other private group entity ❑ government

4a. The following fee(s) are enclosed:

❑ Issue Fee

❑ Publication Fee

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s):

❑ A check in the amount of the fee(s) is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

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Director for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature) (Date)

NOTE; The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Alexandria, Virginia 22313-1450.

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EXAMINER	
ROBINSON, HOPE A	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 02/20/2004

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 402 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 402 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (703) 305-1383. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

PTOL-85 (Rev. 11/03) Approved for use through 04/30/2004.

Notice of Allowability	Application No.	Applicant(s)	
	09/833,041	ROSEN ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *2/6/04*.

2. ☒ The allowed claim(s) is/are *1-21 and 26-29*.

3. ☒ The drawings filed on *08 August 2001* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization of this Examiner's amendment was given in a telephone interview with Mr. Charles Van Horn on February 6, 2004.

3. The claims have been amended as follows:

Please cancel claims 22-25.

Claim 1 (Twice Amended) An albumin fusion protein comprising a member selected from the group consisting of:

(a) a tissue inhibitor metalloproteinase-1 (TIMP-1) protein and albumin, wherein albumin comprises the amino acid sequence of SEQ ID NO:18;

(b) a (TIMP-1) protein and a fragment of the amino acid sequence of SEQ ID NO:18, wherein said fragment has the ability to prolong the shelf-life of the (TIMP-1) protein compared to the shelf-life of the (TIMP-1) protein in an unfused state;

(c) a (TIMP-1) protein and a fragment of the amino acid sequence of SEQ ID NO:18, wherein said fragment has the ability to prolong the shelf-life of the (TIMP-1) protein compared to the shelf-life of the (TIMP-1) protein in an unfused state, and further wherein the said fragment comprises amino acid residues 1-387 of SEQ ID NO:18;

(d) a fragment of a (TIMP-1) protein and albumin comprising the amino acid sequence of SEQ ID NO:18, wherein said fragment has a biological activity of the (TIMP-1) protein;

(e) a (TIMP-1) protein, or fragment thereof and albumin, or fragment thereof, of (a) to (d), wherein the (TIMP-1) protein or fragment thereof, is fused to the N-terminus of albumin or the N-terminus of the fragment of albumin;

(f) a (TIMP-1) protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), wherein the (TIMP-1) protein or fragment thereof, is fused to the C-terminus of albumin, or the C-terminus of the fragment of albumin;

(g) a (TIMP-1) protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), wherein the (TIMP-1) protein or fragment thereof, is fused to the N-terminus and C-terminus of albumin, or the N-terminus and the C-terminus of the fragment of albumin;

(h) a (TIMP-1) protein or fragment thereof, and albumin or fragment thereof, of (a) to (d), which comprises a first (TIMP-1) protein or fragment thereof and a second (TIMP-1) protein or fragment thereof, wherein said first (TIMP-1) protein or fragment thereof is different from said second (TIMP-1) protein or fragment thereof;

(i) a (TIMP-1) protein or fragment thereof, and albumin or fragment thereof, of (a) to (h), wherein the (TIMP-1) protein or fragment thereof, is separated from the albumin or the fragment of albumin by a linker; and

(j) a (TIMP-1) protein or fragment thereof, and albumin or fragment thereof, of (a) to (i), wherein the (TIMP-1) protein or fragment thereof, wherein the albumin fusion protein has the following formula:

R1-L-R2; R2-L-R1; or R1-L-R2-L-R1,

and further wherein R1 is (TIMP-1) factor protein or fragment thereof, L is linker, and R2 is albumin comprising the amino acid sequence of SEQ ID NO:18 or a fragment of albumin.

Claim 2 (Twice Amended) The albumin fusion protein of claim 1, wherein the shelf-life of the albumin fusion protein is greater than the shelf-life of the (TIMP-1) protein or fragment thereof, in an unfused state.

Claim 3 (Twice Amended) The albumin fusion protein of claim 1, wherein the in vitro biological activity of the (TIMP-1) protein or fragment thereof, fused to albumin, or fragment thereof, is greater than the in vitro biological activity of the (TIMP-1) protein or fragment thereof, in an unfused state.

Claim 4 (Twice Amended) The albumin fusion protein of claim 1, wherein the in vivo biological activity of the (TIMP-1) protein or fragment thereof, fused to albumin, or fragment thereof, is greater than the in vivo biological activity of the (TIMP-1) protein or fragment thereof, in an unfused state.

Claim 5 (Twice Amended) An albumin fusion protein comprising a tissue inhibitor metalloproteinase-1 (TIMP-1) protein or fragment thereof, inserted into an albumin, or fragment thereof, comprising the amino acid sequence of SEQ ID NO:18 or fragment thereof .

Claim 6 (Twice Amended) An albumin fusion protein comprising a tissue inhibitor metalloproteinase-1 (TIMP-1) protein or fragment thereof, inserted into an albumin, or fragment thereof, comprising an amino acid sequence selected from the group consisting of:

(a) amino acids residues 54 to 61 of SEQ ID NO:18;

(b) amino acids residues 76 to 89 of SEQ ID NO:18;

(c) amino acids residues 92 to 100 of SEQ ID NO:18;

(d) amino acids residues 170 to 176 of SEQ ID NO:18;

(e) amino acids residues 247 to 252 of SEQ ID NO:18;

(f) amino acids residues 266 to 277 of SEQ ID NO:18;

(g) amino acids residues 280 to 288 of SEQ ID NO:18;

(h) amino acids residues 362 to 368 of SEQ ID NO:18;

(i) amino acids residues 439 to 447 of SEQ ID NO:18;

(j) amino acids residues 462 to 475 of SEQ ID NO:18;

(k) amino acids residues 478 to 486 of SEQ ID NO:18; and

(l) amino acids residues 560 to 566 of SEQ ID NO:18.

Claim 7 (Twice Amended) The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the shelf-life of the (TIMP-

1) protein or fragment thereof, as compared to the shelf-life of the (TIMP-1) protein or fragment, in an unfused state.

Claim 8 (Twice Amended) The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the shelf-life of the (TIMP-1) protein or fragment thereof, as compared to the shelf-life of the (TIMP-1) protein or fragment, in an unfused state.

Claim 9 (Twice Amended) The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vitro biological activity of the (TIMP-1) protein or fragment thereof, fused to albumin as compared to the in vitro biological activity of the (TIMP-1) protein or fragment, in an unfused state.

Claim 10 (Twice Amended) The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vitro biological activity of the (TIMP-1) protein or fragment thereof, fused to albumin as compared to the in vitro biological activity of the (TIMP-1) protein or fragment, in an unfused state.

Claim 11 (Twice Amended) The albumin fusion protein of claim 5, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vivo biological activity of the (TIMP-1) protein or fragment thereof, fused to albumin as compared to the in vivo biological activity of the (TIMP-1) protein or fragment, in an unfused state.

Claim 12 (Twice Amended) The albumin fusion protein of claim 6, wherein said albumin fusion protein comprises a fragment of albumin sufficient to prolong the in vivo biological activity of the (TIMP-1) protein or fragment thereof, fused to albumin as compared to the in vivo biological activity of the (TIMP-1) protein or fragment, in an unfused state.

Claim 13 (Original) The albumin fusion protein of any of claims 1-12, which is non-glycosylated.

Claim 14 (Original) The albumin fusion protein of any of claims 1-12, which is expressed in yeast.

Claim 15 (Original) The albumin fusion protein of any of claim 14, wherein the yeast is glycosylation deficient.

Claim 16 (Original) The albumin fusion protein of any of claim 14, wherein the yeast is glycosylation and protease deficient.

Claim 17 (Original) The albumin fusion protein of any of claims 1-12, which is expressed by a mammalian cell.

Claim 18 (Original) The albumin fusion protein of any of claims 1-12, wherein the albumin fusion protein is expressed by a mammalian cell in culture.

Claim 20 (Original) A composition comprising the albumin fusion protein of any one of claims 1-12 and a pharmaceutically acceptable carrier.

Claim 21 (Original) A kit comprising the composition of claim 20.

Claim 26 (Currently Amended) A method of extending the shelf-life of a tissue inhibitor metalloproteinase-1 (TIMP-1) protein or fragment thereof, comprising the step of fusing the (TIMP-1) protein or fragment thereof, to albumin, or fragment thereof, sufficient to extend the shelf-life of the (TIMP-1) protein, or fragment thereof, compared to the shelf-life of the (TIMP-1) protein, or fragment thereof in an unfused state.

Claim 27 (Original) A nucleic acid molecule comprising a polynucleotide sequence encoding the albumin fusion protein of any one of claims 1-12.

Claim 28 (Original) A vector comprising, the nucleic acid molecule of claim 27.

Claim 29 (Original) A host cell comprising the nucleic acid molecule of claim 28.

4. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

Conclusion

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (571) 272-0957. The examiner can normally be reached on Monday-Friday from 9:00 am to 6:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached at (571) 272-0951.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax

your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope Robinson, MS

Patent Examiner

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER